

Appl. No.: 10/666,311  
Filed: September 18, 2003

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PATENT

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1-9 (Cancelled).

10. (Amended) A method for generating a at least one non-naturally occurring variant protein with at least one desired characteristic relative to a scaffold protein, said method comprising:

a) inputting into a computer a primary library comprising a plurality of first protein sequences and said scaffold protein sequence;

b) aligning said plurality of first protein sequences and said scaffold protein sequence to generate an alignment of sequences having variable residue positions, said alignment generated using an alignment program on said computer;

c) analyzing said alignment to generate a probability distribution of amino acid residues at each each variable residue position, such that each variable residue position has a set of possible amino acids;

d) recombining amino acid residues from said probability distribution at a plurality of variable positions with amino acid residues at non-variable residue positions to generate a secondary library of secondary sequences;

e) computationally ranking said secondary library and eliminating at least one unfavorably ranked sequence from said secondary library to generate a tertiary library, wherein at least one sequence of said tertiary library is different from said primary sequences; and

f) synthesizing a plurality of sequences in said tertiary library and screening said tertiary library to identify at least one non-naturally occurring variant protein with said desired characteristic.

Claim 11 (Cancelled)

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**Claim 12 (Previously Presented):** A method according to claim 11, wherein said synthesizing is done by multiple PCR with pooled oligonucleotides.

**Claim 13 (Previously Presented):** A method according to claim 11, wherein said pooled oligonucleotides are added in equimolar amounts.

**Claim 14 (Previously Presented):** A method according to claim 11, wherein said pooled oligonucleotides are added in amounts that correspond to the frequency of the amino acid residues from said probability distribution.